REMARKS

Amendments to Specification

The instant specification has been amended to recite various trademarks in their proper forms as well as to correct apparent typographic errors. No new matter is introduced to the application as originally filed.

Amendments to Drawings

FIG. 1 has been replaced with FIG. 1 enclosed herewith, which is labeled "Replacement Sheet" in the top margin. The changes to FIG. 1 on file, already discussed above under the section titled "Amendments to the Drawings", are further explained below.

It is noted that the replacement FIG. 1 adds tube (12), cells (20) collected therein, and final composition (30). The final composition (30) includes cells (20) and compounds (22).

It is also noted that in the replacement FIG. 1, compounds (22) have been re-drawn to clearly illustrate that compounds (22) includes an anticoagulant agent (24), a fixative agent (26) and optionally, a polyacrylic acid (28).

It is further noted that in the replacement FIG. 1, the surface of compounds (22) is leveled as compounds (22) are in a liquid form in accordance with the presently claimed invention.

Support for the foregoing amendments to FIG. 1 is clearly found throughout the instant specification as originally filed. No new matter is introduced.

Claim Status

It is first noted that the instant claims have been amended to recite the reference numbers for parts of the device of the present invention, which numbers exactly correspond to those used in the instant specification and drawings as originally filed.

Independent claims 1, 14 and 27 have been amended to recite a collection container (10) or a tube (12) for collecting a final composition (30) having a volume of 100 parts as well as compounds (22) being in a volume of no greater than 2 parts.

New claims 28-29 (both dependent from claim 1) and new claims 34-35 (both dependent from claim 14) have been added, further characterize that the compounds (22) are in a volume of no greater than 1.5 parts, or 1 part.

Support for the above amendments/additions is found at pages 18-19, in paragraph [0022] of the instant specification as well as in original claims 6 and 19 as filed, which teaches that to avoid significant dilution, the compounds 22 (comprising of the anticoagulant agent 24, the fixative agent 26, and optionally, the acid 28) are in concentrated forms, preferably in a ratio with the final composition 30 that is less than about 2:100, more preferably less than about 1.5:100, and most preferably less than about 1:100. Claims 6 and 19 have been cancelled without prejudice.

Additionally, claims 1, 14 and 27 have been amended to refer to mammalian cells. Support for such amendment is obvious from original claims 7 and 20, which further characterize that the cells are selected from whole blood, epithelial cells, bone marrow, spinal fluid, abnormal tissue sample in a cellular suspension, and a combination thereof. Support can also be derived from paragraphs [0007], [0014], [0021], [0022], [0029] and [0031] of the instant specification.

Furthermore, claim 1(d) has been amended to improve clarity. Support for such amendment is clearly found in original claim 1. Claim 14 has been amended to better reflect the present invention. Specifically, claim 14, as amended, clearly indicates that a closure (18) is not a part of the collection container (10). Support for such amendment is clearly found in original claim 1 as well as in paragraphs [0009], [0015], [0029] and FIG. 2 of the instant specification.

Claims 3-4 and 16-17 have been amended for formality reasons that are unrelated to patentability. Support for such amendment is clearly found in original claims 1(b) and 14(b), respectively.

Claims 5 and 18 have been amended to correct typographic or grammatical errors.

Claim 8 has been amended to improve clarity. Support for such amendment is clearly found in original claim 8.

Claim 24 has been amended to improve clarity. Support for such amendment is clearly found in original claim 14(b).

Claims 9, 11-13, 22 and 24-26 have been cancelled without prejudice.

New claims 30-31 have been added, which further characterize that the concentration of the fixative agent (26) preloaded in the tube (12) is less than about 0.75 g/ml, or 0.5 g/ml. Support for these new claims is clearly found at pages 13-14, in paragraph [0019] of the instant specification.

New claims 32-33 have been added, which further characterize that the concentration of the anticoagulant agent (24) preloaded in the tube (12) is less than about 0.2 g/ml, or 0.15 g/ml. Support for these new claims is clearly found at pages 12-13, in paragraph [0018] of the instant specification.

New claims 36-37 have been added, which further characterize that the concentration of the fixative agent (26) positioned within the container (10) is less than about 0.75 g/ml, or 0.5 g/ml. Support for these new claims is clearly found at pages 13-14, in paragraph [0019] of the instant specification.

New claims 38-39 have been added, which further characterize that the concentration of the anticoagulant agent (24) position within the container (10) is less than about 0.2 g/ml, or 0.15 g/ml. Support for these new claims is clearly found at pages 12-13, in paragraph [0018] of the instant specification.

New claims 40-48 have been added, which are directed to a method for preparing whole blood cells for analysis such as HIV screening. Support for these new claims is found throughout the instant specification and original claims as filed.

New claims 49-50 have been added, which are directed to a method of screening a subject for abnormal cells or tissues. Support for these new claims can be found in original claims 25-26 as well as at page 1, in paragraph [0002] and at pages 23-24, in paragraph [0030] of the instant specification.

Applicants respectfully submit that the foregoing amendments do not introduce any new matter to the original application as filed.

New claims 28-39 further characterize the previously elected method or device claims of Group I and fall within the scope of the previously elected invention. As such, Applicant respectfully requests that they be examined together with the previously elected claims of Group I.

New claims 40-48 are directed to a method for preparing whole blood cells for analysis using the device of the present invention. These claims fall within the scope of the

previously elected Group III, as such, Applicant respectfully requests that they be examined together with the previously elected claims of Group III.

New claims 49-50 are directed to a method for screening a subject for abnormal cells or tissues using the device of the present invention. These claims, corresponding to pending claims 25 and 26 (cancelled herein), are patentably related to the previously elected device claims as process of use and product. Since claims 25 and 26 (Group II) have been rejoined to the product claims for examination, new claims 49-50 should also be examined together with the previously elected claims.

With the foregoing amendments, claims 1-5, 7-8, 10, 14-18, 20-21, 23 and 27-50 are currently pending.

Objections to Specification

The instant specification is objected to because of improper use of trademarks. In response, Applicant has amended the specification to recite various trademarks in their proper forms. As such, this objection is overcome.

Claim Objections

Claims 3-6 and 16-19 are objected to because of informalities. In response, Applicant has amended claims 3-5 and 16-18 to correct the typographic or grammatical errors as suggested by the Examiner. Claims 6 and 19 have been cancelled without prejudice. As such, the claim objections are overcome.

Claim Rejection – 35 USC §112, First Paragraph

Claims 1-27 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with enablement requirement. In response, Applicant respectfully traverses this rejection.

It is first noted that the instant claims have been amended to refer to mammalian cells. As acknowledged by the Examiner, the specification enables for products and methods that preserve the morphology and antigenic properties of mammalian cells. As such, the instant claims, as presently amended, are enabled.

Claim Rejection – 35 USC §112, Second Paragraph

Claims 1-27 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. In response, Applicants respectfully traverse this rejection.

In particular, the Examiner states that it is not clear whether the instant claims include cells as a necessary component or not. In response, Applicant respectfully submits that the instant claims, directed to a method of making a device for collecting cells, a device for collecting cells, and downstream applications for the device, do not recite cells as a necessary component of the device. Instead, the instant claims, as amended, recite a collection container (10) or tube (12) for collecting a final composition (30) having a volume of 100 parts as well as to recite compounds (22) preloaded in the container or tube being in a volume of no greater than 2 parts. Also, the amended claims no longer refer to "said cells".

The Examiner rejects the phrase "in a sufficient amount to preserve said cells' original morphology and antigenic sites without significant dilution of said cells" as allegedly being indefinite. In response, it is noted that the above rejected phrase has been removed

from claims 1, 14 and 27. As presently amended, the instant claims recite a collection container (10) or tube (12) for collecting a final composition (3) having a volume of 100 parts as well as to recite compounds (22) preloaded in the container or tube being in a volume of no greater than 2 parts. The amended claims clearly set forth the feature that the amount of the compound is very small relative to the final volume within the container or tube once the sample is drawn. Hence, it is contended that the amended claims clearly define a cell collecting device or method of making/using the same.

The Examiner states that claims 3, 4, 16 and 17 recite concentrations (g/ml), but there is no basis provided in the claims for these comparative limitations. In response, Applicant respectfully submits that as discussed above under the section titled "Claim Status", paragraphs [0018] and [0019] of the instant specification clearly provide the basis for the concentration limitations.

Specifically, paragraph [0018] recites, "[f]or example, in a preferred embodiment, K_3EDTA is the anticoagulant agent 24 and its concentration weight/volume is preferably less than about 0.3 g/ml, more preferably less than about 0.2 g/ml, and most preferably about less than about 0.15 g/ml." Paragraph [0019] recites, "[f]or example, in a preferred embodiment, diazolidinyl urea is the fixative agent 26 and its concentration weight/volume is preferably about less than about 1 g/ml, more preferably less than about 0.75 g/ml, and most preferably less than about 0.5 g/ml concentration of solution of DU before blood sample is added."

Applicant is unclear what the Examiner means when reasoning "there is no basis provided in the claims for these comparative limitations". First, the recited limitations are just the concentrations of the fixative agent (26) or the anticoagulant agent (24). There is no comparison involved. Second, concentrations in unit "g/ml" clearly refer to weight/volume,

as further evidenced from the above descriptions of the instant specification. Third, there is basis provided in claim 1 or 14 for the fixative agent (26) or anticoagulant agent (24). Claims 3, 4, 16 and 17 further characterize the concentrations of the fixative agent (26) or anticoagulant agent (24) that is preloaded in the container (10) or tube (12) before the sample is drawn up. That is, Applicant believes that claims 3, 4, 16 and 17 are clear.

The Examiner states that claims 6 and 19 refer to a ratio between the anticoagulant and the fixative agent in the collection device, but it is not clear whether this ratio is a weight ration, molar ratio, or some other type. In response, Applicant first notes that claims 6 and 19 have been cancelled and the subject matter thereof has been incorporated into their base claims (i.e., claims 1 and 14). As amended, claims 1 and 14 clearly recite a collection container (10) or tube (12) for collecting a final composition (30) having a volume of 100 parts and compounds (22) preloaded in the container (10) or tube (12) being in a volume of no greater than 2 parts. Since the container (10) is described as having "an internal volume of between 100 μl to 10 ml" and the sample is drawn up in volume (*see* paragraph [0016] of the instant specification), it is clear that the ratio referred to in claims 6 and 19 are volume/volume.

Additionally, Applicant respectfully submits that the ratio referred to in claims 6 and 19 are not between the anticoagulant and fixative agent in the collection device, but between the compounds (22) (including the anticoagulant (24) and fixative (26) agents) and the final composition (30) (including the compounds (22) and cells (20) that are drawn up in the container or tube).

The Examiner rejects claim 9 alleging that the phrase "can come into physical contact with said collected and preserved cells" recited therein is confusing. In response, Applicant notes that claim 9 has been cancelled.

The Examiner rejects claims 12 and 25 because of improper use of trade names referring to products. In response, Applicant first notes that claims 12 and 25 have been cancelled and the subject matter thereof has been rewritten into new claims 49-50. Next, Applicant draws the Examiner's attention that the various trade names are not referenced in the new claims.

The Examiner rejects claim 14 alleging that the recitation "an open end and a closed end" with "a closure at said open end of said container" is not clear as to how an end of a tube can be both open and have a closure. In response, Applicant has amended claim 14 to clearly indicate that a closure is not a part of the container, but a part of the device.

The Examiner rejects claim 22 alleging that the phrase "that can come into physical contact with said cells" recited therein is confusing. In response, Applicant notes that claim 22 has been cancelled without prejudice.

The Examiner lastly rejects claims 25 and 26 for improper use claim format. In response, Applicant notes that these claims have been cancelled and rewritten into new claims 49-50, directed to a method of screening a subject for abnormal cells or tissues with method steps recited therein.

In view of the foregoing amendments and remarks, Applicant respectfully submits that the instant claims, as presently amended/added, are definite. As such, the rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

Claim Rejection – 35 USC §101

Claims 25 and 26 stand rejected under 35 U.S.C. §101, as allegedly resulting in an improper definition of a process. In response, Applicants respectfully traverse this rejection.

As discussed above, claims 25 and 26 have been cancelled and rewritten into new claims 49-50. The new claims are directed to a method of screening a subject for abnormal cells or tissues with method steps recited therein. As such, the rejection under 35 U.S.C. §101 should be withdrawn in view of the foregoing amendments.

Claim Rejection – 35 USC §103

Claims 1-4, 6-17 and 19-27 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Ryan (U.S. Patent No. 5,849,517; "**Ryan**") taken in view of Camiener (U.S. Patent No. 5,977,153; "**Camiener**") and Glover et al. (U.S. Patent No. 3,879,295; "**Glover**") and Louderback (U.S. Patent No. 3,973,913: "**Louderback**"). In response, Applicants respectfully traverse this rejection.

- ***Instant invention***

First, it is noted that the instant claims have been amended to recite a collection container (10) or tube (12) for collecting a final composition (30) having a volume of 100 parts as well as to recite compounds (22) preloaded in the container or tube in a volume of no

greater than 2 parts, preferably, no greater than 1.5 parts, and more preferably, no greater than 1 part.

The claimed invention provides a device or a method for collecting and preserving cells in which due to the small amounts of the reagents, there is minimal dilution of the cell sample by reagents such as anticoagulant and fixative agents though stabilization of the resulting drawn blood sample of considerably larger volume is surprisingly achieved. The reagents are concentrated to an extent that when, for example, about 60 µl is placed in the device and 5 ml blood sample then drawn into it, the sample would not be significantly diluted – the dilution error is about 1% (5000 µl / 5060 µl). The claimed invention allows direct treatment of the cells (peripheral blood, bone marrow, etc.) with anticoagulant and fixative reagents as the cell sample is directly drawn into the device, and subsequent direct analysis through flow cytometry.

In summary, as a result of the Applicant's (i) selection of specific compounds; (ii) selection of the recited concentrations; (iii) selection of the small amounts of the compounds; and (iv) the ability to reduce sources of contamination or sample corruption, due to stabilization immediately by direct contact of the reagents with a blood sample during blood draw, it is possible to achieve high integrity blood samples that can be preserved for prolonged transport, such as may occur in an environment where ready access to analyzing instrumentation is not possible.

- ***Prior art***

Ryan

Ryan discloses a method and composition for fixing and stabilizing tissues, cells, and cell components such that the antigenic sites and nucleic acids are preserved. Particularly, **Ryan** discloses applications of diazolidinyl urea (DU) and imidazolidinyl urea (IDU) for the purpose of stabilizing the antigenic sites of samples for phenotyping analysis. **Ryan** discloses the preferred volume ratio of sample to reagent of from about 1:4 to about 2:1, with 1:1 being the most preferred (*see* Col. 5, lines 5-10; Col. 8, lines 35-38 thereof). That is, the sample is diluted 50-400%, with 100% being the most preferred.

Although it teaches the use of EDTA and a fixative like IDU or DU for preserving cells, **Ryan** teaches a different method for preserving the samples. As discussed above, **Ryan** discloses the sample to reagent ratio of from about 1:4 to about 2:1, with 1:1 being the most preferred, which indicates that in **Ryan** the cell samples are diluted at least 50% by mixing with the fixative reagents. In contrast, the instant application teaches a method of preserving cells in which there is a minimal dilution of the sample by the reagents, as indicated by the volume ratio of sample to reagent being 100:≤2, preferably 100:≤1.5, and more preferably 100:≤1. That is, **Ryan** does not teach the reagents in small volumes and high concentrations.

Neither does **Ryan** teach direct blood draw. In fact, **Ryan**, which is one of Applicant's earlier patents, involves first drawing a cell sample into a collection tube containing anticoagulant agents (e.g., K_3 EDTA vacutainer), and then transferring a portion of the sample from the first tube to a second tube containing an equal volume of fixative agents as described in the Specific Example I thereof. That is, the anticoagulant agents and

fixative agents are in separate containers, and the cell sample is not drawn directly into the container containing fixative agents. Hence, the blood sample is not in direct contact with the fixative agents during the blood draw. Since the process disclosed in **Ryan** does not involve directly drawing blood sample into a container containing fixative agents, **Ryan** is not faced with the same problem of maintaining stability of a direct blood draw for remote transport of the sample as that faced in the claimed invention. As a result, **Ryan** does not teach the same method/device as that of the present invention.

Camiener

Camiener discloses a solid or powered preservative/fixative composition and a process for preserving, fixing or stabilizing biological material for microscopic examination using the composition thereof. In particular, **Camiener**'s composition comprises a reactive group-containing agent (e.g. DU) and a polar group-containing stabilizing compound (e.g. citric acid). Further, **Camiener** teaches that their fixative, preservative or embalming solutions comprises an aldehyde or antimicrobial compound or a combination thereof.

Although citric acid can function as an anticoagulant at some concentrations, there is no need for an anticoagulant to exist for the composition as claimed in **Camiener**. Also, there is no teaching or suggestion in **Camiener** to use their composition for stabilizing / preserving cells (e.g. whole blood cells) for flow cytometric analysis.

Glover

Glover teaches a tissue collection device that holds a vacuum inside and may be sealed (*see* Abstract). **Glover** also teaches adding a clotting agent after the blood sample is collected to obtain serum (*see* Col. 6, lines 53-55), or alternatively, adding an anticoagulant

agent if plasma is desired (*see* Col. 6, lines 61-64). In either case, **Glover** does not teach preloading the clotting or anticoagulant agent in the collection device before the sample is collected.

Louderback

Louderback discloses a stable blood control standard. Although teaching that EDTA is an anticoagulant, **Louderback** does not teach or suggest a device for collecting cells, comprising both anticoagulant and fixative agents in small volumes so that there is minimal dilution of the cells by reagents though stabilization of the resulting drawn blood sample of considerably larger volume.

- ***Instant invention is not obvious over prior art***

The problems to be solved in the instant invention are related to the field of preserving and analyzing cells (especially flow cytometric analysis) in the clinical world, especially in developing countries where limited access to clinical laboratories for reliable diagnosis of diseases is available, which include: (1) limited ability to collect and analyze patient samples due to lack of transportation, refrigeration and instruments; (2) cells collected and preserved using conventional methods and instruments generally require further dilution and/or treatment before they can be analyzed by flow cytometry. However, any significant dilution of the sample is likely to cause error in flow cytometry measurements (e.g., lowering the lymphocytes' count); (3) conventional methods are inadequate in that the samples have to be analyzed soon after collection; and (4) conventional methods involve the use of toxic, flammable and carcinogenic reagents for fixing and stabilizing cells.

The claimed invention solves all of the above-mentioned problems as described in paragraph [0008] of the instant specification:

> The claimed subject matter addresses many of the challenges encountered when using conventional methods and instruments to collect and preserve cells by providing a method and a collection device that are capable of maintaining the cells in their original unaltered morphology; preserving the cell antigenic sites; and allowing the cells to be transported at ambient temperature, to be handled in a low toxicity and non-flammable environment, and to be directly analyzed by flow cytometry without further dilution and/or treatment. The claimed subject matter more specifically relates to a method and a device that allow cells (e.g., whole blood, epithelial cells, spinal fluid, and the like.) to be collected and preserved for analysis and addresses many of the challenges encountered when using conventional methods and instruments. Specifically, the claimed subject matter describes a method and a collection device that (1) use a less toxic and non-flammable reagent for fixing and stabilizing cells; (2) allow the cells to stay in their original unaltered morphology; (3) allow the cell antigenic sites to be preserved for a useful period of time; (4) allow the cells to be transported at ambient temperature; and/or (5) allow the cells to be directly analyzed by flow cytometry without further dilution and/or treatment. *Id.*

In detail, the solutions provided by the claimed invention involve using low toxic, non-flammable and non-carcinogenic fixative agent such as DU, IDU or both; drawing a final composition (including a cell sample) having a volume of 100 parts into a collection container which contains less than 2 parts of reagents including anticoagulant and fixative agents; storing the sample with the reagents for more than about 3 days, preferably more than about 5 days, and more preferably more than about 7 days; transporting the sample with the reagents in the container at ambient temperature from the collection site to the analysis site; directly analyzing the sample by flow cytometry without further dilution and/or treatment of the sample.

Furthermore, the problems to be solved in the instant invention also include finding a way to achieve effective stabilization of samples with only a small amount of fixative, and in

the presence of other reagents. The prior art did not have the constraints upon it as did Applicant. Specifically, prior art used larger amounts of fixative, and did not need to be concerned about interactions with other reagents or with other whole blood components that direct blood draw conditions impose. The solution of the instant invention is provision of a way to stabilize direct draw blood samples for long-range transport. The result is surprising in that such a small amount of the reagents works effectively well. It is also surprising that there is no adverse interaction with other reagents. It is further surprising that the blood sample itself can function as a diluent.

- ***Comments to Examiner's Arguments***

At page 11 of the present Office Action, the Examiner alleges (1) a person of ordinary skill in the art would have had a reasonable expectation of success in including the dried DU of **Camiener** within the EDTA-containing evacuated device of **Ryan** for the purpose of preserving cells; (2) a person of ordinary skill in the art would have had a further expectation of success in employing the evacuated tissue collection device of **Glover** as the "vacutainer" of **Ryan**; and (3) a person of ordinary skill in the art would have had a further reasonable expectation of success in combining the teachings of **Ryan** and **Glover** because **Louderback** teaches that EDTA prevents clotting. In response, Applicant respectfully submits the following remarks.

Even if one skilled in the art would be motivated to use **Camiener**'s Vacutainer System for preserving a tissue sample using the composition and method of **Ryan**, he or she still would not have arrived at the instantly claimed invention because neither reference solves the problem of significant dilution of the sample prior to cytometry analysis, which

problem is likely to cause error in flow cytometry measurements (e.g., lowering the lymphocytes' count).

In detail, although the prior art as described in **Ryan** might appear to solve some of the above-mentioned problems, for example, problems (3) and (4), by using low toxic and non-flammable fixative agents such as IDU and DU, **Ryan** does not solve the other problems, for example, problem (2) because **Ryan**'s method significantly dilutes the sample (e.g., with a dilution of at least 50%).

Additionally, **Glover** clearly teaches away from the present invention, because it teaches that clotting agent should be added once blood has been collected. That is, one skilled in the art, when motivated by **Glover**'s teaching, would not have preloaded an anti-clotting agent (anticoagulant agent) in the collection tube before the blood sample is collected.

Further, the Examiner alleges, at page 11, that the selection of the amount of DU and EDTA to include in the collection device would have been a routine matter of optimization on the part of the artisan of ordinary skill. In response, Applicant respectfully disagrees. As discussed above, **Ryan** teaches diluting the cell samples at least 50% by mixing with the fixative reagents, whereas the instant application teaches preserving cells with a minimal dilution by the reagents at the volume ratio of sample to reagent being 100:≤2, preferably 100:≤1.5, and more preferably 100:≤1. That is, **Ryan** does not teach the reagents in small volumes and high concentrations.

None of the secondary references cited by the Examiner, **Camiener**, **Glover**, or **Louderback**, compensates the deficiency of **Ryan**'s as discussed above. The routine matter of optimization as alleged by the Examiner would have to come from the teaching of **Ryan**, which actually teaches away from the present invention as already discussed above. The

present invention, using reagents in small volumes and high concentrations for preserving cells for direct cytometry analysis, is changing the way flow cytometry is used in the environments where the ability to collect and analyze patient samples is limited due to lack of transportation, refrigeration and instruments.

In view of the foregoing amendments and remarks, Applicant submits that **Ryan** further in view of **Camiener**, **Glover** and **Louderback** do not render the claimed invention obvious. As such, the obviousness rejection under 35 U.S.C. §103(a) should be withdrawn.

Claims 5 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over **Ryan**, **Camiener**, **Glover** and **Louderback** as applied to Claims 1-4, 6-17 and 19-27 above, and further in view of Deich et al. (U.S. Patent No. 5,110,908; "**Deich**").

Claims 5 and 18, dependent from claims 1 and 14, respectively, further characterize the method and device of the present invention. As a result of the dependency, all of the technical features included in claims 1 and 14 are carried over to claims 5 and 18.

As discussed above, **Ryan** in view of **Camiener**, **Glover** and **Louderback** do not render claims 1 and 14 obvious.

Deich discloses haemophilus influenzae peptides and proteins. Although teaching that polyacrylic acid is an adjuvant suitable for use in vaccine production, **Deich** does not compensate the above-mentioned deficiencies of **Ryan**, **Camiener**, **Glover** and **Louderback**. That is, **Deich** does not teach using reagents in small volumes and high concentrations for preserving cells for direct cytometry analysis.

Even if one skilled in the art were motivated to include a polyacrylic acid in the collection device to facilitate the production of vaccines after combining the teachings of all of the above-cited references, he or she still would not have arrived at the present invention

as claimed because the above references do not lead to the collection device or method of making/using the device as claimed in the present invention.

In view of the foregoing amendments and remarks, Applicant submits that **Ryan** in view of **Camiener**, **Glover** and **Louderback**, and further in view of **Deich**, do not render the claimed invention obvious. As such, the obviousness rejection under 35 U.S.C. §103(a) should be withdrawn.

Nonstatutory Double Patenting Rejection

Claims 27 stand rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 7, 8, 12 and 13 of **Ryan** in view of **Glover**. In response, Applicants respectfully traverse this rejection.

As provided by MPEP 804, double patenting may exist between an issued patent and an application filed by the same inventive entity, or by a different inventive entity having a common inventor, and/or by a common assignee/owner. In this case, although **Ryan** and the instant application are filed by a common inventor and owned by a common assignee, **Glover** is filed by a different inventive entity that does not share a common inventor with the instant application or being owned by a common assignee. As such, **Glover** is improperly cited for the present nonstatutory double patenting rejection.

The same section of MPEP further provides that "[a] nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s)", and that "[o]bviousness-type double patenting requires rejection of an application claim when the claimed subject matter is **not patentably distinct**

from the subject matter claimed in a commonly owned patent, or a non-commonly owned patent but subject to a joint research agreement as set forth in 35 U.S.C. 103(c)(2) and (3), when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent." As already discussed above, **Ryan** provides a different method/device for collecting cells from that of the present invention. In particular, instant claim 27 provides a method for preparing cells for analysis by providing a container for collecting a final composition having a volume of 100 parts, which container has anticoagulant and fixative agents preloaded therein in a volume of no greater than 2 parts. **Ryan** does not teach preloading anticoagulant and fixative agents in small volumes in the same container before a cell sample is drawn. That is, **Ryan** does not anticipate instant claim 27. Additionally, **Ryan** teaches diluting the cell sample with fixative agent by at least 50%, which is a teach-away from instant claim 27 as discussed above.

In view of the foregoing remarks, it is contended that the nonstatutory obviousness-type double patenting rejection is not proper. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

Other Remarks

At page 15 of the present Office Action, the Examiner requests that Applicant specifically point out the support for any amendments made to the disclosure, including the claims, by referring to pages and line numbers in the as-filed specification, not the published application. As requested, Applicant has done so under the section titled "Claim Status".

Further at the same page, the Examiner requests that Applicant provides a list of all co-pending U.S. applications that set forth similar subject matter to the present claims and

share an inventor or assignee with the instant application. In response, Applicant notes that no such co-pending application exists in the U.S.

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This document is filed concurrently with a petition for a one-month extension of time. The Commissioner is authorized to deduct the extension fees of $130 from Howrey Deposit Account No. 08-3038/12642.0065.NPUS01. Should any additional fees be required for any reason, the Commissioner is authorized to deduct such fees from the same Deposit Account.

Respectfully submitted,

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